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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:		Confirmation No.:	7314
Richard A. PITTNER *et al.*		Art Unit:	1646
Appln. No.:	10/016,969	Examiner:	Ruixiang LI
Filed:	December 14, 2001	Atty. Docket:	18528.010 / 0401-UTL-0
Title:	PEPTIDE YY AND PEPTIDE YY AGONISTS FOR TREATMENT OF METABOLIC DISORDERS		

APPELLANTS' BRIEF

Mail Stop **Appeal Brief – Patents**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Further to the Notice of Appeal and the Pre-Appeal Brief Request for Review filed on October 2, 2006 for the above-captioned application, Appellants submit this Brief on Appeal.

1. Real Party in Interest

The real party in interest is Amylin Pharmaceuticals, Inc., a California corporation with offices at 9360 Towne Centre Drive, San Diego, California 92121.

2. Related Appeals and Interferences

Appellants have not identified any related appeals or interferences that would have a bearing on the Board's decision in the present appeal.

3. Status of Claims

Claims 33, 43-47, 51, and 54-73 are pending and under consideration. Claims 1-32, 34-42, 48-50, and 52-53 were previously canceled, and claim 74 is canceled in an amendment filed concurrently herewith.

Claims 33, 43-46, 51, and 54-74 stand finally rejected under 35 U.S.C. § 112, first paragraph as lacking enablement and written description. Claims 33, 43-47, 51, 54-72 and 74 stand finally rejected under 35 U.S.C. § 112, second paragraph as being indefinite, and claims 33, 47, 54, 56-60, 62, 64, 71, 72, and 74 stand rejected under 35 U.S.C. § 103(a) as obvious.

Appellant appeals each of these rejections of the claims under 35 U.S.C. §§ 112, first paragraph, 112, second paragraph, and 103(a).

Claims 73 and 74 have additionally been objected to due to alleged informalities. An amendment after final has been submitted herewith to correct these minor informalities.

4. Status of Amendments

An amendment after final is submitted concurrently herewith canceling dependent claim 74 and correcting minor informalities noted in the claim objections. Such amendment merely corrects errors noted by the Examiner in the final office action, does not require further search and consideration, and removes issues on appeal. Following entry of the amendment filed concurrently with the present Appeal Brief, the objections to claims 73 and 74 are moot.

5. Summary of the Claimed Subject Matter

The claimed invention relates to methods for reducing food intake, appetite, nutrient availability, caloric efficiency, weight, or weight gain, or a method of increasing weight loss. As

explained in the specification, in certain aspects, it has been surprisingly discovered that the peripheral administration of PYY and agonists thereof have a potent effect to reduce nutrient availability, reduce food intake, suppress appetite, reduce weight gain, decrease caloric efficiency, *etc*. See, *e.g*., published specification, para. **[0031]**, **[0032]**, examples 6 and 7, *etc*.

Any suitable PYY or PYY agonist may be useful in the invention, *e.g.*, useful as agents to reduce nutrient availability, including reduction of food intake, *etc*. Preferred PYY agonists include peptide agonists, particularly PYY agonist analogs such as PYY[3-36]. Analogs may be made by, *e.g.*, conservative amino acid substitution of the sequence of PYY or portions thereof, and can be tested in the assays provided in the Examples or other suitable assays that distinguish the actions of PYY from those of NPY or PP Non-peptide agonists are also contemplated. See, *e.g.*, *id.* at paras. **[0034]**-**[0041]**. Particular considerations for identifying PYY agonists useful in the methods of the present invention are discussed in further detail in the specification, *e.g.*, at paragraphs **[0050]**-**[0053]**.

A. Independent Claim 56

Independent claim 56 sets forth steps for a method of reducing food intake. See, *e.g.*, *id.* at para. **[0033]**. The claimed method generally comprising peripherally administering to a subject (see, *e.g.*, *id.*), via a parenteral route (see, *e.g.*, *id.* at para. **[0044]**), an amount of PYY agonist analog effective to reduce food intake. In accordance with the claim, the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids (see, *e.g.*, *id.* at Table 1 and para. **[0034]**), and the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor (see, *e.g.*, *id.* at para. **[0033]**).

B. Independent Claim 55

Independent claim 55 sets forth method steps similar to independent claim 56, but specifically recites that the subject is a human subject (see, *e.g.*, *id.* at para. **[0048]**).

C. Independent Claim 65

Independent claim 65 also sets forth method steps similar to independent claim 56, but specifically recites that the subject has a condition or disorder which can be treated by reducing food intake (see, *e.g.*, *id.* at para. **[0017]**, **[0019]**, *etc.*).

D. Independent Claim 43

Independent claim 43 sets forth method steps similar to independent claims 56 and 55, but additionally recites that the amount of PYY agonist analog administered comprises about 5 µg to 100 µg per day in a single or divided dose (see, *e.g.*, *id.* at para. **[0047]**).

E. Independent Claim 44

Independent claim 44 sets forth method steps similar to independent claims 56 and 55, but additionally recites that the amount of PYY agonist analog administered comprises about 0.1 µg/kg to 10 µg/kg per day in a single or divided dose (see, *e.g.*, *id.* at para. **[0047]**).

F. Independent Claim 69

Independent claim 69 again sets forth method steps similar to claim 56. However, claim 69 recites a method of reducing food intake and body weight (see, *e.g.*, *id.* at para. **[0018]**, **[0031]**, **[0032]**, example 6, *etc.*). Further, as in independent claim 65, claim 69 specifically recites that the subject has a condition or disorder which can be treated by reducing food intake and body weight (see, *e.g.*, *id.* at para. **[0017]**, **[0019]**, *etc.*).

G. Independent Claim 57

Independent claim 57 again sets forth method steps similar to claim 56. However, claim 57 recites a method of reducing appetite (see, *e.g.*, *id.* at para. **[0046]**, **[0047]**, Table 1, *etc.*).

H. Independent Claim 45

Independent claim 45 sets forth method steps similar to independent claim 57, but specifically recites that the subject is a human subject (see, *e.g.*, *id.* at para. **[0048]**).

I. Independent Claim 67

Independent claim 67 also sets forth method steps similar to independent claim 57, but specifically recites that the subject has a condition or disorder which can be treated by reducing appetite (see, *e.g.*, *id.* at para. **[0017]**, **[0019]**, *etc.*).

J. Independent Claim 46

Independent claim 46 sets forth method steps similar to independent claims 57 and 45, but additionally recites that the amount of PYY agonist analog administered comprises about 0.1 µg/kg to 10 µg/kg per day in a single or divided dose (see, *e.g.*, *id.* at para. **[0047]**).

K. Independent Claim 58

Independent claim 58 sets forth method steps similar to claim 56. However, claim 57 recites a method of reducing nutrient availability (see, *e.g.*, *id.* at para. **[0013]**, **[0017]**, **[0032]**, *etc.*).

L. Independent Claim 66

Independent claim 66 sets forth method steps similar to independent claim 58, but specifically recites that the subject has a condition or disorder which can be treated by reducing nutrient availability (see, *e.g.*, *id.* at para. **[0017]**, **[0019]**, *etc.*).

M. Independent Claim 64

Independent claim 64 sets forth method steps similar to claim 56. However, claim 64 recites a method of reducing caloric efficiency (see, *e.g.*, *id.* at Example 7, *etc.*).

N. Independent Claim 68

Independent claim 68 sets forth method steps similar to claim 56. However, claim 68 recites methods for reducing weight, reducing weight gain, or increasing weight loss (see, e.g., id. at Example 6, Example 7, para. **[0113]**, *etc*. Further, claim 68 specifically recites that the subject has a condition or disorder which can be treated by reducing weight, reducing weight gain or increasing weight loss (see, *e.g.*, *id.* at para. **[0017]**, **[0019]**, *etc.*).

6. Grounds of Rejection to be Reviewed on Appeal

1. Whether claims 33, 43-46, 51, and 54-74 are unpatentable under 35 U.S.C. § 112, first paragraph as lacking written description.

2. Whether claims 33, 43-46, 51, and 54-74 are unpatentable under 35 U.S.C. § 112, first paragraph as lacking enablement.

3. Whether claims 33, 43-47, 51, 54-72 and 74 are unpatentable under 35 U.S.C. § 112, second paragraph as being indefinite.

4. Whether claims 33, 47, 54, 56-60, 62, 64, 71, 72, and 74 are unpatentable under 35 U.S.C. § 102(b) as anticipated over Yoshinaga *et al.* (*Am. J. Physiol.* 263:G695-701 (1992)) (hereinafter "Yoshinaga").

7. Argument

A. Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

1. *Claims 33, 43-46, 51, and 54-74*

Claims 33, 43-46, 51, and 54-74 stand rejected under 35 U.S.C. § 112, First Paragraph as allegedly lacking written description. Reversal of this rejection is respectfully requested.

In support of this rejection, the Examiner alleges that "the specification fails to provide any critical structural feature to adequately describe the genus of PYY agonists that may be administered in the claimed method. The specification merely discloses two compounds, a human PYY of SEQ ID NO:2 and PYY (3-36) of SEQ ID: NO:3, which are not sufficiently representative of the genus of PYY agonists." *Office Action* at page 5. The Examiner goes on to state that "only the method of administering PYY and PYY (3-36), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph." *Office Action* at page 6. Applicants respectfully disagree with these assertions.

The standard for determining whether a claim drawn to a genus meets the written description requirement is clear. "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice . . . , reduction to drawings . . . , or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." See *Regents of the University of California v. Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406; M.P.E.P § 2163(II)(3)(a)(ii) (emphasis added). Applicants have met this burden.

What constitutes a "representative number" of species is an inverse function of the skill and knowledge in the art. *Capon v. Eshhar,* 418 F.3d 1349 (Fed. Cir. 2005). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Description of a representative number of species does not require the description to be of such

specifics that it would provide individual support for each species that the genus embraces. "That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation." *Falkner v. Inglis*, 448 F.3d, 1357, 1366 (Fed Cir. 2006). Also relevant to the analysis is the claimed invention, and the context of the genus within the claimed invention.

In this regard, the present invention is directed to various methods for reducing food intake, appetite, nutrient availability, caloric efficiency, weight, or weight gain, or a method of increasing weight loss. As explained in the specification, in certain aspects it has been surprisingly discovered that the peripheral administration of PYY and agonists thereof have a potent effect to reduce nutrient availability, reduce food intake, suppress appetite, reduce weight gain, decrease caloric efficiency, *etc.* See, *e.g.*, published specification, para. **[0031]**, **[0032]**, examples 6 and 7, *etc.* Thus, the scope of the genus of PYY compounds is viewed in the context of the claimed method, and the disclosure of species within the genus is understood by those skilled in the art based on the scope of teachings related to the claimed methods.

Any suitable PYY or PYY agonist may be useful in the invention, *e.g.*, useful as agents to reduce nutrient availability, including reduction of food intake, *etc.* However, the data demonstrate greater pharmacological effects relevant to the claimed methods at various Y receptors given specific structural and functional attributes of the specific PYY compound. See, *e.g.*, *id.* at para. **[0033]**, Table 1, *etc.* Based in part on these findings, the claims recite a genus of PYY compounds wherein the PYY compound is a PYY agonist analog that is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids and which elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. It is noted that for biomolecules, receptor specificity can be used to meet the written description requirement. See, *MPEP* §2163 II A 3 (a). As such, the claims are drawn to specific methods, and define a specific genus of compounds useful in those methods based, at least in part, on specific teachings in the specification with regard to specific structural and functional attributes common to the genus of compounds. As in *Capon* and *Falkner*, it is noted that the

claims are not drawn to a novel genus of compounds, but rather to novel uses of those compounds based at least in part on the identification of common structural and functional attributes of those compounds, as claimed in the present therapeutic methods.

Nonetheless, further written description support for the genus of compounds useful in the claimed methods may be found in the specification though disclosure and teachings of concepts of PYY agonist analogs. For instance, the specification states that "PYY agonist analogs" refer to any compound structurally similar to a PYY that has PYY activity typically by virtue of binding to or otherwise directly or indirectly interacting with a PYY receptor or other receptor or receptors with which PYY itself may interact or elicit a biological response. Such compounds include derivatives of PYY, extended PYY molecules having more than 36 amino acids, truncated PYY molecules having less than 36 amino acids, and substituted PYY molecules having one or more different amino acids, or any combination of the above. Such compounds may also be modified by processes such as amidation, glycosylation, acylation, sulfation, phosphorylation, acetylation and cyclization. See, *e.g.*, *id.*, para. **[0015]**.

Moreover, it is noted that such PYY agonist analogs were generally known at the time of filing, as recognized by those skilled in the art. For instance, see U.S. Patent No. 5,604,203 in Example 2. It is now well-established that the binding precedent of the Federal Circuit "does *not* set forth a *per se* rule that whenever a claim limitation is directed to a macromolecular sequences, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art *Falkner* at 1367 (emphasis in original) Indeed the Federal Circuit has held that requiring patentees to recite known sequences would serve no goal of the written description requirement. *Id*, at 1368. Nonetheless, the specification provides additional disclosure, teaching that PYY analogs may be made by, *e.g.*, conservative amino acid substitution of the sequence of PYY or portions thereof, and can be tested in the assays provided in the Examples or other suitable assays that distinguish the actions of PYY from those of NPY or PP. See, *e.g.*, *id.* at paras. **[0034]**-**[0041]**. Particular considerations for identifying PYY agonist analogs useful in the methods of the present invention are discussed in further detail in the specification, *e.g.*, at paragraphs **[0050]**-**[0053]**.

The Examiner asserts that the claims do not provide "a structural feature of the recited PYY agonist analogs because it merely excludes PY [sic] from the amino acid sequences of PYY

agonist analogs, but does not indicate what structure the PYY agonist analogs have." Applicants respectfully traverse. Again, the specification provides more than sufficient guidance as to the scope of the structure of PYY agonist analogs, particularly in light of the knowledge of those skilled in the art. Such analogs are structurally similar to PYY, and, *e.g.*, interact with a PYY receptor. Further, PYY analogs are made by conservative amino acid substitution of the sequence of PYY, as generally understood by those skilled in the art. Thus, in additional to the structural limitation recited in the claim, i.e., that the first two N-terminal amino acids are not YP, the PYY agonist analogs recited in the claims are understood to be structurally limited in accordance with the teachings of the specification and the general knowledge of those skilled in the art.

In support of the rejection, the Examiner also asserts that the limitation of "wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5, or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor" does not provide a definitive functional limitation for the PYY agonist analogs because it involves two varying factors. Again, Applicants respectfully traverse. As recited in the claim and understood by those skilled in the art, such a limitation functionally defines the genus of PYY agonist analogs based on a single comparator pharmacological effect, as related across Y receptor types. The magnitude of this pharmacological effect may certainly be functionally compared across Y receptor types to functionally define a PYY agonist analog, as recited in the claims. The specification, and in particular Table 1, is replete with citations to literature comparing the activities of different pancreatic polypeptides at various receptors and for different pharmacological effects. This extensive literature demonstrates that, contrary to the assertions of the Examiner, those skilled in the art are routinely able to compare the effects of PYY molecules at different receptors.

Based on the scope of such teachings, the knowledge in the art, and the context of the claim invention, it is submitted that Applicants have provided more than adequate guidance as to structural and functional characterization of the PYY compounds useful in the claimed methods to those skilled in the art to sufficient describe the invention commensurate in scope with the present claims. Accordingly, Applicants submit that PYY agonist analogs useful in the claimed methods are sufficiently described in the specification so to reasonably convey to one of ordinary

skill in the art that the inventors, at the time the application was filed, had possession of the therapeutic methods of the claimed invention.

Applicants respectfully submit that one skilled in the art would readily appreciate that Applicants, at the time of the filing of the present application, were in possession of the methods of the claimed invention, including the recited genus and, therefore, have met the written description requirement. As such, it is submitted that the claims comply with 35 U.S.C. §112, first paragraph, and reversal of this rejection is respectfully requested.

2. *Claim 73*

Claim 73 was also rejection under 35 U.S.C. §112, first paragraph as alleged lacking written description. Reversal of this rejection is respectfully requested.

In support of the rejection, the Examiner asserts that the limitation "wherein the pharmacological effect at the Y1 receptor is an increase in blood pressure" introduces new matter. The Examiner alleges that there is not sufficient support for the limitation at page 21, lines 10-12, as pointed out by Applicants. Applicants respectfully traverse.

Again, the specification clearly cites measurement of blood pressure, see, *e.g.*, Example 5, and it was known in the art at he time of filing that the Y1 receptor mediates vasoconstriction and blood pressure increase, see, *e.g.*, page 10, col. 1 and page 14, col. 2 of the Gehlert reference cited in Table 1 with regard to the properties of Y receptor activities.

In this regard, the subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. *See* M.P.E.P. § 2163.02. Taken as a whole, one of skill in the art would understand the inventors to be in possession of measurement of blood pressure as a pharmacological effect, and measurement of that effect at the Y1 receptor. As such, it is submitted that claim 73 is fully supported by the specification as filed, and does not introduce new matter. Reversal of this rejection is therefore respectfully requested.

B. Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 33, 43-46, 51, and 54-74 stand rejected under 35 U.S.C. § 112, First Paragraph as allegedly lacking enablement commensurate in scope with the claims. Reversal of this rejection is respectfully requested.

The Examiner acknowledges that the specification is enabled for the use of PYY or PYY(3-36) in the claimed methods. *Final Office Action* mailed July 26, 2006 at page 4. However, in support of the rejection, the Examiner asserts that the specification "does not reasonably provide enablement for methods of administering a genus of PYY agonist analogs." *Id.*

Applicants respectfully traverse for at least the reasons which follow. Initially, it is submitted that the Examiner has not met the evidentiary burden to impose an enablement rejection for failure to enable one of skill to use the invention. A specification that discloses how to make and use a claimed invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995) (*quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (CCPA. 1971) (emphasis in original)).

Applicants have provided ample direction and guidance, and have presented numerous examples of compounds that activate Y receptors within the context of the claimed pharmacological effects, such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. *See* Specification, for example, in paras. **[0031]-[0033]**, Table 1, *etc.* The Examiner has not provided sufficient evidence to cast doubt on the guidance provided in the specification in this regard. Rather, the Examiner has focused strictly on the number of working examples and jumped to a conclusion that the working examples provided do not adequate guide on "how to make the genus of PYY agonist analogs and thus how to use the instantly claimed invention." *Final Office Action* mailed July 26, 2006 at page 5.

Again, it is noted that the claims are drawn to novel methods of using a class of PYY compounds. The specification demonstrates that PYY compounds with specific structural and functional activity will have specific pharmacological activity. Applicants have recited such structural and functional limitations in the claims to define a genus of PYY compounds particularly useful in the claimed methods. Further, the specification has provided detailed guidance with regard to testing methodologies for identifying and confirming the pharmacological activity of PYY compounds within the scope of the recited genus. In this

regard, the law provides that experimentation is not necessarily undue simply because it is complex, if the art typically engages in such experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174, (Int'l Trade Comm'n 1983) *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985); *Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006).

For instance, given the knowledge in the art, and based on the guidance provided in the specification regarding Y receptors and methodologies for determining whether a PYY compound elicits a claimed pharmacological activity, additional PYY agonist analogs can be identified within the context of the present claims without the need for undue experimentation. The Examiner's attention is respectfully drawn to the description that provides guidance, particularly to a person of skill in the art. The specification at paragraphs **[0033]** describe activity at various Y receptors along with Table 1, and paragraphs **[0049]-[0053]** generally describe screening assays. These teachings along with the literature cited throughout the specification, particularly in Table 1, establish that screening for activity at various receptors is routine in the art. The examples provide further guidance for determining the efficacy of compounds in methods within the scope of the present claims. Based on such guidance, one of skill in the art would be able to practice the claimed invention with only routine experimentation.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and reversal of this rejection is respectfully requested.

C. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 33, 43-47, 51, 54-72, and 74 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Reversal of this rejection is respectfully requested.

In support of the rejection, the Examiner alleges that the claims are indefinite due to the recitation of the limitation "wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5, or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor" in that it allegedly involves two varying factors. Again, Applicants respectfully traverse. As discussed above, such a limitation functionally defines the genus of PYY agonist analogs based on a single comparator

pharmacological effect, as related across Y receptor types. One of skill in the art would certainly understand the metes and bounds of this claim limitation in the context of the teachings of the specification and the claimed therapeutic methods, and would have no difficulty performing such comparisons.

Further, the Examiner asserts that the term "a pharmacological effect" is ambiguous. Again, one of skill in the art would certainly understand the metes and bounds of the claim terminology in the context of the claimed methods and the teachings of the present specification, particularly with regard to the pharmacological activities of the recited Y receptors with regard to the specifically claimed therapeutic methods, *e.g.*, food intake, appetite, nutrient availability, *etc.*

It is noted that claim 74 was also rejected due to the alleged informality of the recitation of the acronym "PP." This claim is cancelled in the Amendment After Final submitted concurrently herewith. Upon entry of the amendment, this rejection is moot.

1. *Dependent Claim 47*

More particularly, dependent claim 47 recites that the PYY agonist analog is PYY[3-36]. The comparative activity of PYY[3-36] at various Y receptors with regard to, *e.g.*, PYY, is specifically provided in the specification, for instance at Table 1. Moreover, the specification and data and examples of numerous pharmacological effects of PYY[3-36]. Based on such description, one of skill in the art would certainly understand the metes and bounds of the claim terminology in the context of the claimed methods and the teachings of the present specification, particularly with regard to the pharmacological activities of the recited Y receptors with regard to the specifically claimed therapeutic methods, *e.g.*, food intake, appetite, nutrient availability, *etc.*

As such, it is submitted that the claims terms are definite, and that the claims comply with 35 U.S.C. § 112, second paragraph. Reversal of this rejection is therefore respectfully requested.

D. Rejection Under 35 U.S.C. § 102(b)

Claims 33, 47, 54, 56-60, 62, 64, 71, 72, and 74 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yoshinaga. Reversal of this rejection is respectfully requested.

It is well established that to anticipate a claim, a reference must disclose every element of the claim. *Verdegaal Bros. v. Union Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989). Applicants submit that

cited prior art fails to disclose each and every element of the present claims, and therefore does not anticipate the claimed invention.

In rejecting the claims at issue, the Final Office Action asserts that the claimed methods are anticipated by the teachings of Yoshinaga. The Office Action describes Yoshinaga teaching a method of inhibiting pancreatic exocrine and gastric acid output, which are "necessarily linked to other properties of PYY or PYY agonists, such as caloric efficiency, nutrient availability, appetite, food intake or weight (see bottom of instant specification)." *Final Office Action* mailed July 26, 2006, page 9-10. In further support of the rejection, the Office Action asserts that the intended uses and properties of the PYY agonist analog recited in the claims are inherent to the method taught by Yoshinaga, and that the property or functional activity is inherent to the structure of a molecule because it is well established that a property or function of a molecule depends upon its structure. The Office Action then continues "[i]t is noted that recognition by a person of ordinary skill in the art is not required to show anticipation by inherency." *Id.* at page 10. Again, Applicants respectfully traverse.

1. *Independent Claim 56 and those Dependent Therefrom*

Independent claim 56 is directed to methods for reducing food intake in a subject in need thereof. As discussed in previous responses, Yoshinaga is completely silent with regard to food intake. Rather, as acknowledged in the Office Action, Yoshinaga discuses methods for inhibiting pancreatic exocrine and gastric acid output. That the agents disclosed by Yoshinaga are inherently capable of functioning in the methods claimed in the present application does not render the present claims unpatentable over the teachings of Yoshinaga. In this regard, it is noted that the claims are directed to specific methods of use not recognized in the cited prior art, rather than compositions of matter possessing the inherent property or functional activity.

Again, the claims at issue require a method for reducing food intake in a subject in need thereof. The Federal Circuit has directly addressed this issue of claim interpretation, and held that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose. [. . .] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed." *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) (*citations omitted*).

In interpreting a claim directed to a "method of treating macrocytic-megaloblastic anemia in… a human in need thereof," the Federal Circuit held that the claim preamble is a limiting "statement of intentional purpose." *Jansen v. Rexall Sundown,* 342 F.3d at 1333. The Court explained that "administering the claimed vitamins in the claimed doses for some purpose other than treating or preventing macrocytic-megaloblastic anemia is not practicing the claimed method." "[T]he combination of folic acid and vitamin B[12] must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia." *Jansen v. Rexall Sundown,* 342 F.3d at 1334.

In accordance with proper claim interpretation, the present claims require a method comprising the peripheral administration of the specifically recited PYY compounds for the intended purpose of reducing food intake to a subject with a recognized need for administration. The mere disclosure in Yoshinaga of the administration of PYY(3-36) to dogs for the purpose of inhibiting pancreatic exocrine and gastric acid output does not amount to a teaching or suggestion of the claimed methods.

As mentioned above, nothing in Yoshinaga teaches or suggests a method of reducing food intake, or a subject in need of such methods. Absent a teaching of a need for intervention in the reduction food intake, one of skill in the art would simply find no motivation to perform a method as recited in the present claims for the specific intended purpose of such claims.

Nonetheless, the Examiner asserts that there is a link between the use disclosed by Yoshinaga and the claimed methods such that the intended uses and properties "of the PYY agonist analog (PYY(3-36)) recited in the claims are inherent to the methods taught by Yoshinaga." Again, it is noted that the claims are drawn to methods, not compositions. Thus, the inherent properties of the recited PYY agonist analogs are not relevant. The required elements of the recited methods that must be taught by the reference are at issue. Moreover, as provided in the response previously filed on May 17, 2006, the parameters measured in Yoshinaga are not necessarily and always linked to reduction of food intake. In studying other peptide hormones, gastric acid secretion and gastric emptying were not always correlated with effects on food intake and satiety (see Jin, Conover, Muurahainen, previously cited).

As the cited art does not disclose each and every element of independent claim 56, it is submitted that independent claim 56, and the claims dependent therefrom, are patentable over the prior art of record, and reversal of this rejection is respectfully requested.

2. *Independent Claim 57 and those Dependent Therefrom*

Independent claim 57 is directed to methods for reducing appetite in a subject in need thereof. As discussed in previous responses, Yoshinaga is completely silent with regard to appetite. Rather, as acknowledged in the Office Action, Yoshinaga discuses methods for inhibiting pancreatic exocrine and gastric acid output. Again, the claims at issue require a method for reducing appetite in a subject in need thereof. The Federal Circuit has directly addressed this issue of claim interpretation, and held that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose. [. . .] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed." *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) (*citations omitted*).

In accordance with proper claim interpretation, the present claims require a method comprising the peripheral administration of the specifically recited PYY compounds for the intended purpose of reducing food intake to a subject with a recognized need for administration. The mere disclosure in Yoshinaga of the administration of PYY(3-36) to dogs for the purpose of inhibiting pancreatic exocrine and gastric acid output does not amount to a teaching or suggestion of the claimed methods.

As mentioned above, nothing in Yoshinaga teaches or suggests a method of reducing appetite, or a subject in need of such methods. Absent a teaching of a need for intervention in the reduction of appetite, one of skill in the art would simply find no motivation to perform a method as recited in the present claims for the specific intended purpose of such claims.

Nonetheless, the Examiner asserts that there is a link between the use disclosed by Yoshinaga and the claimed methods such that the intended uses and properties "of the PYY agonist analog (PYY(3-36)) recited in the claims are inherent to the methods taught by Yoshinaga." Again, it is noted that the claims are drawn to methods, not compositions. Thus, the inherent properties of the recited PYY agonist analogs are not relevant. The required

elements of the recited methods that must be taught by the reference are at issue. Moreover, as provided in the response previously filed on May 17, 2006, the parameters measured in Yoshinaga are not necessarily and always linked to reduction of appetite. In studying other peptide hormones, gastric acid secretion and gastric emptying were not always correlated with effects on food intake and satiety (see Jin, Conover, Muurahainen, previously cited).

As the cited art does not disclose each and every element of independent claim 57, it is submitted that independent claim 57, and the claims dependent therefrom, are patentable over the prior art of record, and reversal of this rejection is respectfully requested.

3. *Independent Claim 58 and those Dependent Therefrom*

Independent claim 58 is directed to methods for reducing nutrient availability in a subject in need thereof. As discussed in previous responses, Yoshinaga is completely silent with regard to nutrient availability. Rather, as acknowledged in the Office Action, Yoshinaga discuses methods for inhibiting pancreatic exocrine and gastric acid output. Again, the claims at issue require a method for reducing nutrient availability in a subject in need thereof. The Federal Circuit has directly addressed this issue of claim interpretation, and held that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose. [. . .] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed." *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) (*citations omitted*).

In accordance with proper claim interpretation, the present claims require a method comprising the peripheral administration of the specifically recited PYY compounds for the intended purpose of reducing nutrient availability to a subject with a recognized need for administration. The mere disclosure in Yoshinaga of the administration of PYY(3-36) to dogs for the purpose of inhibiting pancreatic exocrine and gastric acid output does not amount to a teaching or suggestion of the claimed methods.

As mentioned above, nothing in Yoshinaga teaches or suggests a method of reducing nutrient availability, or a subject in need of such methods. Absent a teaching of a need for intervention in the reduction of nutrient availability, one of skill in the art would simply find no

motivation to perform a method as recited in the present claims for the specific intended purpose of such claims.

Nonetheless, the Examiner asserts that there is a link between the use disclosed by Yoshinaga and the claimed methods such that the intended uses and properties "of the PYY agonist analog (PYY(3-36)) recited in the claims are inherent to the methods taught by Yoshinaga." Again, it is noted that the claims are drawn to methods, not compositions. Thus, the inherent properties of the recited PYY agonist analogs are not relevant. The required elements of the recited methods that must be taught by the reference are at issue. Moreover, as provided in the response previously filed on May 17, 2006, the parameters measured in Yoshinaga are not necessarily and always linked to reduction of nutrient availability. In studying other peptide hormones, gastric acid secretion and gastric emptying were not always correlated with effects on food intake and satiety (see Jin, Conover, Muurahainen, previously cited).

As the cited art does not disclose each and every element of independent claim 58, it is submitted that independent claim 58, and the claims dependent therefrom, are patentable over the prior art of record, and reversal of this rejection is respectfully requested.

4. *Independent Claim 64 and those Dependent Therefrom*

Independent claim 64 is directed to methods for reducing caloric efficiency in a subject in need thereof. As discussed in previous responses, Yoshinaga is completely silent with regard to caloric efficiency. Rather, as acknowledged in the Office Action, Yoshinaga discuses methods for inhibiting pancreatic exocrine and gastric acid output. Again, the claims at issue require a method for reducing caloric efficiency in a subject in need thereof. The Federal Circuit has directly addressed this issue of claim interpretation, and held that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose. [. . .] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed." *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) (*citations omitted*).

In accordance with proper claim interpretation, the present claims require a method comprising the peripheral administration of the specifically recited PYY compounds for the intended purpose of reducing caloric efficiency to a subject with a recognized need for

administration. The mere disclosure in Yoshinaga of the administration of PYY(3-36) to dogs for the purpose of inhibiting pancreatic exocrine and gastric acid output does not amount to a teaching or suggestion of the claimed methods.

As mentioned above, nothing in Yoshinaga teaches or suggests a method of reducing caloric efficiency, or a subject in need of such methods. Absent a teaching of a need for intervention in the reduction of caloric efficiency, one of skill in the art would simply find no motivation to perform a method as recited in the present claims for the specific intended purpose of such claims.

Nonetheless, the Examiner asserts that there is a link between the use disclosed by Yoshinaga and the claimed methods such that the intended uses and properties "of the PYY agonist analog (PYY(3-36)) recited in the claims are inherent to the methods taught by Yoshinaga." Again, it is noted that the claims are drawn to methods, not compositions. Thus, the inherent properties of the recited PYY agonist analogs are not relevant. The required elements of the recited methods that must be taught by the reference are at issue. Moreover, as provided in the response previously filed on May 17, 2006, the parameters measured in Yoshinaga are not necessarily and always linked to reduction of caloric efficiency. In studying other peptide hormones, gastric acid secretion and gastric emptying were not always correlated with effects on food intake and satiety (see Jin, Conover, Muurahainen, previously cited).

As the cited art does not disclose each and every element of independent claim 64, it is submitted that independent claim 64, and the claims dependent therefrom, are patentable over the prior art of record, and reversal of this rejection is respectfully requested.

For at least these reasons, all of the claims are believed to be patentable over the art of record, and reversal of the rejection is respectfully requested.

CONCLUSION

Appellant believe that the above discussion is fully responsive to all grounds of rejection set for in the application. Please deduct the requisite fee of $500 pursuant to 37 C.F.R. § 1.17(c) from Deposit Account No. 50-2387 and any additional fees that may be due in association with the filing of this Brief.

In particular, it is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in the documents accompanying

this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account Number 50-2387, referencing docket number 18528.010. Applicants likewise authorize a charge to Deposit Account Number 50-2387 for any other fees related to the present application that are not otherwise provided for in the accompanying documents.

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the outstanding rejections of the claims, and that the subject application be allowed forthwith.

Respectfully submitted,

Date: February 5, 2007

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CLAIMS APPENDIX

Claims 1-32. (Canceled)

33. (Previously Presented) The method of any one of claims 43 to 46, 55 to 58, and 64 to 69, wherein the PYY agonist analog has a potency in at least one food intake or gastric emptying assay greater than NPY.

34-42. (Canceled)

43. (Previously Presented) A method of reducing food intake comprising peripherally administering to a human subject, via a parenteral route, an amount of PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 5 μg to 100 μg per day in a single or divided dose.

44. (Previously Presented) A method of reducing food intake comprising peripherally administering to a human subject, via a parenteral route, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 0.1 μg/kg to 10 μg/kg per day in a single or divided dose.

45. (Previously Presented) A method of reducing appetite comprising peripherally administering to a human subject, via a parenteral route, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36]

at a Y1 receptor, and wherein the amount comprises about 5 µg to 100 µg per day in a single or divided dose.

46. (Previously Presented) A method of reducing appetite comprising peripherally administering to a human subject, via a parenteral route, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 0.1 µg/kg to 10 µg/kg per day in a single or divided dose.

47. (Previously Presented) The method according to any one of claims 43 to 46, 55 to 58, and 64 to 69, wherein the PYY agonist analog is PYY[3-36].

48-50. (Canceled)

51. (Previously Presented) The method according any one of claims 43 to 46, 55 to 58, and 64 to 69, further comprising administration of a GLP-1, an exendin, an amylin, a leptin, their agonists, or any combination thereof.

52-53. (Canceled)

54. (Previously Presented) The method according to any one of claims 43 to 46, 55 to 58, and 64 to 69, wherein the PYY agonist analog is administered by an intravenous, intraperitoneal, intramuscular, subcutaneous, topical, nasal or pulmonary inhalation route of administration.

55. (Previously Presented) A method of reducing food intake comprising peripherally administering to a human subject who desires to reduce food intake, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY

agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

56. (Previously Presented) A method of reducing food intake comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

57. (Previously Presented) A method of reducing appetite comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

58. (Previously Presented) A method of reducing nutrient availability comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of PYY agonist analog effective to reduce nutrient availability, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

59. (Previously Presented) The method according to any one of claims 55 to 58 and 64 to 69 wherein the amount of PYY agonist analog is from about 1 μg to about 5 mg per day in a single or divided doses.

60. (Previously Presented) The method according to any one of claims 55 to 58 and 64 to 69 wherein the amount of PYY agonist analog is from about 5 μg to 100 μg per day in a single or divided doses.

61. (Previously Presented) The method according to any one of claims 55 to 58 and 64 to 69 wherein the amount of PYY agonist analog is from about 0.1 μg/kg to 10 μg/kg per day in a single or divided doses.

62. (Previously Presented) The method according to any one of claims 43 to 46, 55 to 58 and 64 to 69 wherein the PYY agonist analog has a higher affinity for either the Y2 or Y5 receptor than for the Y1 receptor.

63. (Previously Presented) The method of any one of claims 56-58 and 64-69, wherein the subject is a human.

64. (Previously Presented) A method of reducing caloric efficiency comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of a PYY agonist analog effective to reduce caloric efficiency, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

65. (Previously Presented) A method of reducing food intake comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing food intake, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

66. (Previously Presented) A method of reducing nutrient availability comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing nutrient availability, an amount of a PYY agonist analog effective to reduce nutrient availability, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

67. (Previously Presented) A method of reducing appetite comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing appetite, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

68. (Previously Presented) A method of reducing weight, reducing weight gain, or increasing weight loss comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing weight, reducing weight gain or increasing weight loss, an amount of a PYY agonist analog effective to reduce weight, reduce weight, reduce weight gain or increase weight loss, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

69. (Previously Presented) A method of reducing food intake and body weight comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing food intake and body weight, an amount of a PYY agonist analog effective to reduce food intake and body weight, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist

analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

70. (Previously Presented) The method of any one of claims 64-69, wherein the disorder is an eating disorder, a reproductive disorder, obesity, insulin-resistance, hypertension, atherosclerosis, dyslipidemia, cardiovascular risk, stroke, congestive heart failure, gallbladder disease, osteoarthritis, sleep apnea, or diabetes mellitus of any kind.

71. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the PYY agonist analog activates a Y2 or Y5 receptor greater than a Y1 receptor.

72. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the PYY agonist analog elicits a pharmacological effect at a Y7 receptor greater than that of NPY.

73. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the pharmacological effect at the Y1 receptor is an increase in blood pressure.

74. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the PYY agonist analog is not PP.

EVIDENCE APPENDIX

NONE

RELATED PROCEEDINGS APPENDIX

NONE